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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,154	12/26/2001	Toshiaki Tagawa	P21462	2932

7055 7590 12/16/2002

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RESTON, VA 20191

EXAMINER

COUNTS, GARY W

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 12/16/2002

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/926,154

Applicant(s)

TAGAWA ET AL.

Examiner

Gary W. Counts

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-- **Th MAILING DATE of this communication app ars on the cov r sh et with the correspond nce address --**
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Status of the claims

The amendment filed on September 24, 2002 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 3 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3, line 2 "sufficient" is vague. It is unclear what is considered to be sufficient. There is no definition or guidance provided for the term in the specification.

Claim 9, line 2 "a marker molecule" is vague and indefinite. It is unclear what applicant intends. There is no definition or guidance for the term in the specification.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

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(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

4. Claims 1, 4-6, and 8-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Allen et al (US 5,527,528).

Allen et al disclose liposomes (microparticle) containing an anti-tumor compound in liposome entrapped form. Allen et al disclose monoclonal antibodies coupled to the liposome by polyethylene glycol chains (col 2). Allen et al disclose that these antibodies are specific for tumor-associated antigens and provides for localizing the liposome at the tumor site (non-free target). Allen et al disclose that that the antibody may be attached to the liposome by covalent or noncovalent attachment methods (col 9, lines 29-30).

With respect to the free target as recited in the instant claims. Allen et al disclose the use of a monoclonal antibody which is specific for a particular tumor epitope and therefore the antibody would have an affinity for the non-free target even in the presence of free targets.

5. Claims 1, 4, 9, 13, 16, and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Buechler et al. (US 6,156,521).

Buechler et al disclose an antibody conjugate comprising an antibody (ligand) coupled to a signal generating element (col 3, lines 20-22). Buechler et al disclose that this signal generating element can be particles (col 8, lines 20-28). Buechler et al disclose that the antibody specifically binds to specific regions of a form of troponin (analyte) or a group of analyte forms (col 3). Buechler et al further disclose that the

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antibody can be a sensitive antibody which binds specifically to a target such that it will exhibit a preferential detection of one form or group of forms of troponin in an immunoassay, and it will have a greater affinity for something it specifically binds than for something it does not specifically bind (col 7). Buechler et al disclose that the antibody (ligand) will preferentially recognize a ternary complex of troponin (non-free target) in the presence of both free troponin I and T (free target) (col 18). Buechler et al disclose that the antibodies can be conjugated to the signal generators in a variety of ways using heterobifunctional reagents.

With respect to the dissociation constant between the target and one ligand as recited in the instant claims. Buechler et al disclose the ligand-bonded complex as claimed and therefore, it would inherently comprise the dissociation constant between the target and one ligand as recited in the instant claims.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 2, 3, and 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buechler et al in view of Nichtl et al (US 5,972,720).

See above for teachings of Buechler et al.

Buechler et al differ from the instant invention in failing to teach a water-soluble macromolecule is bonded to the microparticle.

Nichtl et al disclose particles to the surface of which biomolecules are absorbed, wherein the composition additionally contains polyethylene glycol. Nichtl et al disclose that this composition can be used as a detection reagent in immunological test methods such as for troponin. Nichtl et al disclose that polyethylene glycols substituted by thiol are excellently suitable for the stabilization of biomolecule particle conjugates and as a results of the stronger binding of the substituted polyethylene glycols to the particle surface compared to stabilizers of the state of the art a substantial improvement is achieved with regard to the stability of the conjugates thus leading to an improved long-term stability and a lower aggregation tendency in solution to a better stability towards changes in the environmental conditions and an improved test function (col 2).

It would have been obvious to one of ordinary skill in the art to incorporate polyethylene glycol as taught by Nichtl et al into the ligand complex of Buechler et al because Nichtl et al discloses that polyethylene glycols substituted by thiol are excellently suitable for the stabilization of biomolecule particle conjugates and as a results of the stronger binding of the substituted polyethylene glycols to the particle surface compared to stabilizers of the state of the art a substantial improvement is achieved with regard to the stability of the conjugates thus leading to an improved long-term stability and a lower aggregation tendency in solution to a better stability towards changes in the environmental conditions and an improved test function.

With respect to the number of ligands bonded to the microparticle as recited in the instant claims, the optimum number of ligands can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, it has long been

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settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

8. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Allen et al in view of Lindhofer et al (US 6,294,167).

See above for teachings of Allen et al.

Allen et al differ from the instant invention in failing to teach the ligand-bonded complex in a pharmaceutical composition.

Lindhofer et al disclose immunoliposomes which have monoclonal antibodies bound on their surfaces. Lindhofer et al disclose that these immunoliposomes are contained in pharmaceutical compositions (col 6). Lindhofer et al disclose that these compositions provide for particular tumor cells, to be distinguished from other cells on account of the recognition of specific marker antigens and are therefore suitable for immunological cell therapy and the pharmaceutical compositions lend themselves to in vivo and in vitro therapy of different tumor types (col 1).

It would have been obvious to one of ordinary skill in the art to incorporate pharmaceutical compositions as taught by Lindhofer et al with the liposomes of Allen et al

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because Lindhofer et al shows that these compositions provide for particular tumor cells, to be distinguished from other cells on account of the recognition of specific marker antigens and are therefore suitable for immunological cell therapy and the pharmaceutical compositions lend themselves to in vivo and in vitro therapy of different tumor types.

Response to Arguments

Applicant's argument (filed September 24, 2002) that there is no motivation in the applied art to combine the Benz et al reference and the Wands et al reference, is found persuasive and therefore, the rejection has been withdrawn. However, newly applied references Allen et al (US 5,527,528) and Buechler et al (US 6,156,521) are applied to the pending claims.

See above for teachings of Allen et al and Buechler et al.

Conclusion

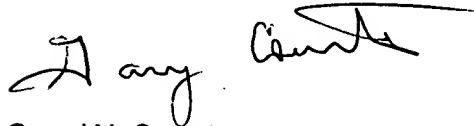
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

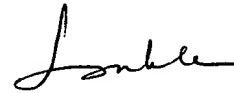
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)3084242 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Gary W. Counts
Examiner
Art Unit 1641
December 2, 2002



LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

12/10/02